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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/580,384	05/20/96	STEINEMANN	T D5715D

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15M1/1014

EXAMINER
KISHORE,G

ART UNIT	PAPER NUMBER
1502	7

DATE MAILED: 10/14/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 6-18-97

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 22-29

Of the above, claim(s) _____ is/are pending in the application.

☐ Claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 22-29 is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON F

DETAILED ACTION

The request for the extension of time and amendment filed on 6-18-97 are acknowledged.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galin or Iverson in combination with Bang and Esmon.

Galin teaches that the anticoagulant, heparin inhibits blood clotting and inflammation of eye (note the abstract, columns 2-3 and claims). Galin however, does not teach the use of Protein C.

Iverson teaches that the intraocular fibrin formation during vitrectomy is inhibited by heparin (note the abstract and page 405). Iverson does not specifically teach the use of protein C.

Esmon teaches that Tumor necrosis factor (TNF) causes inflammatory changes at the endothelial cells and also stimulates microvascular thrombosis (note column 3, line 65 through col. 4, line 13). Esmon further teaches that activated protein C reduces the production of TNF (col. 4, line 41 et seq.).

Bang teaches that protein C enhances the lysis of fibrin. Bang further teaches that the activated protein C is a novel antithrombotic agent with wider therapeutic index than available anticoagulants such as heparin and will be more effective and less likely to cause bleeding complications than heparin (note col. 1, line 23 through col. 2, line 33; col. 18, line 56 et seq., col. 19, line 33 et seq.).

The references of Galin and Iverson clearly show the use of heparin for the inhibition of inflammation of eye and fibrin formation. The reference of Esmon teaches that protein C reduces the amounts of TNF which is responsible for the formation of clots (fibrin), adhesion of PMNs, blood monocytes and subsequent inflammation. The reference of Bang shows the superiority of protein C over heparin. The use of protein C which is known to decrease TNF which is the cause of fibrin formation and the inflammation instead of heparin would have been obvious to an artisan since Bang teaches its superiority.

Applicants' arguments have been fully considered, but are not found to be persuasive.

Applicants' arguments regarding the formation of the thrombin-thrombomodulin complex and the subsequent fibrin formation cascade of reactions are not found to be persuasive since first of all instant claims are drawn to a method of treatment of inflammation and not the pathway leading to the antithrombotic effect. Furthermore, the cascade of chemical reacti ns and the subsequent fibrin f rmation is a vascular phenomenon and not dependent on the tissue. Indeed the cascade f reactions argued by

applicants is elegantly discussed on col. 1, line 36 through col. 2, line 30. It is clearly evident from these lines that protein C is anti thrombotic irrespective of the tissue in which the blood vessels are located.

Applicants argue that in many instances systemically administered drugs do not reach the eye in therapeutic levels. The examiner completely agrees with this statement, but points out that this could true even in this instance because what is shown in the instant disclosure is the effectiveness of protein C upon intraocular injection only and not systemic administration. One would reasonably expect protein C which has wider therapeutic index than available anti-coagulants according to Bang, to be more effective than heparin taught by Iverson upon similar intraocular administration. Furthermore, based on similar logic, one could argue that the reduction of fibrin will not result in the treatment of the disease itself as recited in claims 13 and 16. What is being treated is perhaps one of the conditions (or symptoms of the disease).

3. Claims 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galin or Iverson in combination with Bang and Esmon as applied to claims 22-27 above, and further in view of Stocker.

The primary references do not teach the use of protein S in addition.

Stocker while disclosing the use of protein C activators teaches that protein S potentiates the action of protein C (note the abstract, column 1, lines 16-19).

The use of protein S in addition, would have been obvious to one of ordinary skill in the art because of the potentiating effect taught by Stocker.

Applicants' arguments with regard to the primary references have been addressed by the examiner above. Applicants provide no specific arguments with regard to Stocker.

4. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-5408.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-2351.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1500

gsk

October 1, 1997